

REMARKS

The Office Action of July 8, 2003 presents the examination of claims 1-10, 14, and 15. Claims 3 and 4 are amended. The amendment to claim 4 corrects a typographical error. No new matter is added to the application.

Request for Interview

Upon receipt of this Reply, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at 703-205-8000 to schedule a personal interview at the Examiner's convenience.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner maintains the rejection of claim 3 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not enabled by the specification. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

In the Office Action, the Examiner points out that claim 3 as previously presented does not limit the type of mutation in the conserved regions of p53. In response to the Examiner's remarks, claim 3 is amended to recite that a frameshift or

nonsense mutation in a conserved region II and V of p53 is indicative of poor patient outcome whereas a missense mutation in a conserved region III and IV is indicative of positive patient outcome.

On page 3, lines 9-19 of the specification, it is stated that approximately 70% of mutations in p53 are missense mutations that change the identity of an amino acid and alter the confirmation and stability of p53. Further, on page 7, lines 32-38, it is stated that mutations in p53 that give rise to transcriptional stop signals and a truncated protein (i.e., frameshift and nonsense mutations) prevents p53 from employing its DNA proof-reading role. Finally, on page 8, lines 3-10, it is stated that mutations detrimental to the patient are those which affect the DNA binding or transactivation, whereas those mutations less harmful for the patient are amino acid changes not greatly affecting structure or function of p53 (i.e., missense mutations).

Applicants respectfully submit that claim 3 fully complies with the requirements of 35 U.S.C. § 112, first paragraph (enablement). Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. §§ 102, 103

The Examiner maintains the rejection of claim 15 under 35 U.S.C. § 102(e) for allegedly being anticipated by Vogelstein '676 (USP 5,527,676). The Examiner also maintains the rejection of claims 1, 2, 4-10, and 14 under 35 U.S.C. § 103(a) for allegedly being obvious over Vogelstein '676, in view of Elledge et al. and Callahan et al., and further in view of Hedrum et al. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

In the Reply after Final filed on September 26, 2002, Applicants pointed out that Vogelstein '676 failed to disclose a method for prognostication of the development of neoplasia, but rather disclosed a method for diagnosing a neoplastic tissue of a human. Applicants further pointed out that one skilled in the art recognized the differences between prognostication and diagnosis.

In response, the Examiner asserts that Vogelstein '676 does teach prognostication because Vogelstein '676 discloses that mutations in the short arm of chromosome 17 are responsible for progression of benign disease into malignant carcinoma. The Examiner further relies on the disclosure of Vogelstein '676

that delineation of the molecular events mediating the transition from benign disease into malignant carcinoma is of considerable importance since precursor adenomas are curable whereas carcinomas are lethal.

While it may be true that Vogelstein '676 discloses that delineation of the molecular events mediating the transition from benign disease into malignant carcinoma is important, the fact remains that Vogelstein '676 and the other references cited by the Examiner fail to disclose sequencing exons 2-11 of p53, as recited in claim 15. Instead, Vogelstein '676 discloses sequencing the entire p53 coding region.

In summary, Vogelstein '676 fails to disclose or suggest the prognostication of the development of neoplasia. Further, Vogelstein '676 fails to associate the metastatic potential of the neoplasia based upon the presence, position, and type of mutation. Nor does Vogelstein '676 suggest that certain mutations in p53 are indicative of poor patient outcome. Instead, Vogelstein '676 merely provides the skilled artisan with methods for assessing p53 in human tumors.

As such, Vogelstein '676 fails to anticipate or render obvious the present invention. Further, Elledge et al. and Callahan et al. fail to detect p53 mutations by sequencing exons

2-11 of the gene, whereas Hedrum et al. merely teaches the sequencing of exons 4-9. Thus, absolutely no reference teaches a method for prognostication of the development of neoplasia by sequencing exons 2-11 of p53.

As such, the present invention is not unpatentable over the combination of references cited by the Examiner. Withdrawal of the instant rejection is therefore respectfully requested.

Summary

Overall, the present invention possesses significant patentable features that the cited prior art references do not possess. Furthermore, Applicants submit the instant claims are fully in compliance with 35 U.S.C. § 112, first paragraph. All of the present claims define patentable subject matter such that this application should be placed into condition for allowance. Favorable action on the merits of the present application is thereby requested.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to December 8, 2003, in which to file a reply to the Office Action. The required fee of \$420.00 is attached to the Notice of Appeal, which is being filed concurrently herewith.

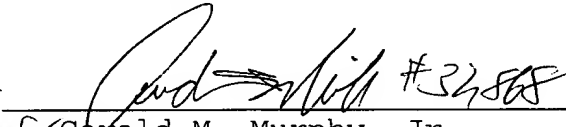
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If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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